

Alzheimer's Disease Fight Focuses on Preventive Treatment

Delaying Onset by Five Years Could Greatly Reduce the Number of Patients

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Studies are finding evidence that changes in diet and exercise can help delay Alzheimer's disease.

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"Earlier is better" has become a mantra in the field of Alzheimer's disease. Experts are targeting the prevention or delay of memory decline more, instead of just focusing on treating patients who have the disease.

Results from one of the largest randomized prevention trial to date presented Sunday here at the Alzheimer's Association International Conference suggest why scientists are thinking this way. The trial found that intervention involving

exercise, diet and other behavioral changes significantly improved overall cognitive functioning in patients after two years, compared with patients in a control group.

The trial, conducted in Finland and known as Finger, is only one of roughly 25 such studies under way, experts say. More are set to begin, examining different preventive strategies in cognitively normal people or those exhibiting mild memory problems who are at high risk for developing dementia.

Some focus on lifestyle activities and others on medications to slow or stop the ravages of the disease on brain tissue and neurons.

The largest involve thousands of participants and cost tens if not hundreds of millions of dollars funded by combination of the government, private foundations and pharmaceutical companies. The latest partnership is expected to be announced Tuesday, with Novartis AG providing significant funding to the Banner Alzheimer's Institute in Phoenix for a prevention trial starting next year likely to cost over \$100 million. The National Institutes of Health is also providing over \$30 million for the study.



Gerry Sampson, chair of the Alzheimer's Association board of directors, speaks at the 2014

Alzheimer's Association International Conference Sunday in Copenhagen. *Associated Press*
The number of Alzheimer's sufferers in the U.S. is expected to roughly triple between 2010 and 2050, growing to 13.5 million in 2050 from 5.1 million in 2010. If the disease could be delayed by just five years, the number of people with Alzheimer's at age 65 in 2050 could be reduced by nearly six million people, according to a report published by the Alzheimer's Association in 2010.

Globally, one-third of Alzheimer's disease is related to risk factors that can be potentially changed, such as lack of education and exercise, according to a study published Monday in the journal *Lancet Neurology*.

"Forestalling the appearance of symptoms by five to 10 years would have a tremendous public health impact and essentially would allow people to live the rest of their lives without real symptoms," says Laurie Ryan, chief of the Dementias of Aging branch at the National Institute on Aging.

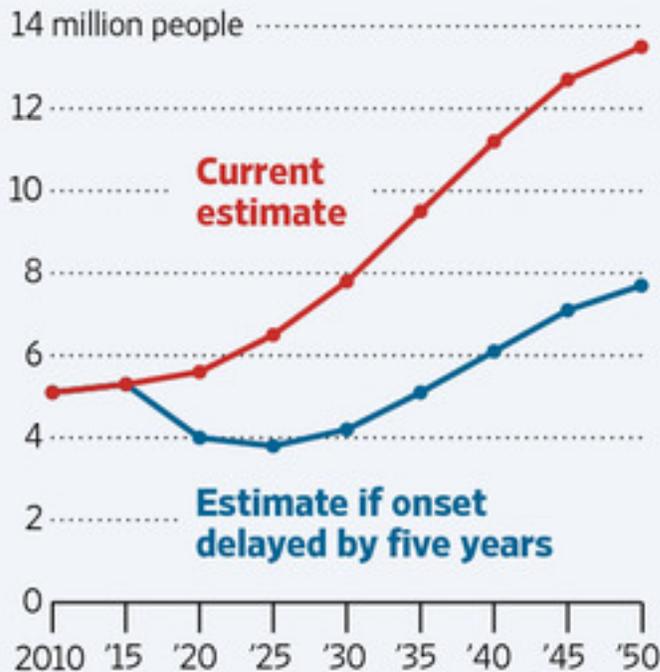
Prevention efforts are receiving more attention and financial backing in the field because of growing recognition in recent years that disease-related changes in the brain begin decades before memory problems become obvious. Treating patients once the symptoms begin may be too late to make a major impact on the disease, as demonstrated by the failure of several highly anticipated experimental treatments in recent years.

Also, a greater ability to measure the progression of the disease in the brain through the use of biological markers, such as the imaging of disease-related proteins, has made it easier to detect the subtle and slow progression of the disease in live humans. Before these biomarker tests, Alzheimer's was diagnosed solely based on clinical symptoms. (It often still is.) Its pathology in the brain could only be examined with autopsy.

However, the studies are challenging because they require following a large number of people for years.

Growth Forecasts

Americans age 65 and older expected to have Alzheimer's disease, 2010-50



Source: Alzheimer's Association
The Wall Street Journal

There have been many previous prevention efforts over the past decade. Many of them were small and most failed, experts say. In 2009, at a meeting convened by the NIH to examine the state of science in Alzheimer's disease, an independent review committee found no compelling evidence to show the disease could be prevented with lifestyle interventions.

Now, however, the mood of the field is shifting toward prevention. Many experts are "cautiously optimistic" about such efforts, according to Pierre Tariot, director of the Banner Alzheimer's Institute.

Several animal studies suggest that administering treatment earlier in the disease could be helpful, according to the NIA's Dr. Ryan.

And recent data from Eli Lilly & Co.'s clinical trial of its experimental compound solanezumab showed that though the compound failed overall to improve cognition in people with Alzheimer's, there was evidence that participants with more mild symptoms of the disease did benefit.

The Finger trial presented Sunday randomly assigned 1,260 people ages 60 to 77. Some went to a control group and were given basic health advice. Others underwent an intervention that incorporated diet and exercise, cognitive training, social activities and control of physical risk factors like high blood pressure and cholesterol.

After two years, those in the intervention group had significantly improved performance on different memory measures compared with the control group,

according to Miia Kivipelto, a professor of clinical geriatric epidemiology at Karolinska Institutet in Stockholm, who presented the work. The participants will continue to be followed for seven years.

Several trials in the field are testing compounds thought to reduce in the brain the amount of a protein called amyloid as preventive strategies. Clumps of the protein, known as plaques, are thought to contribute to the disease.

One Banner study expected to begin in 2015 and take nine years to complete will focus on 1,300 cognitively normal people with mutations in the ApoE4 gene, which put them at higher risk of the disease, and test two different anti-amyloid drugs, Dr. Tariot says.

There's also the 5,800-participant Tommorrow study, funded by Takeda Pharmaceutical Co. and Zinfandel Pharmaceuticals Inc., to examine whether a diabetes drugs called pioglitazone may delay symptoms in the next five years in people at high risk as predicted by a combination of age and a gene called TOMM40, who are cognitively normal.

"The general feel in the field is that it's all in the timing," says Kathleen A. Welsh-Bohmer, director of the Joseph & Kathleen Bryan Alzheimer's Disease Center at Duke University, who leads the design of the neuropsychological measures used in the Tommorrow study.

While a lot of animal data and human epidemiological data showing that people who engage in healthy lifestyle practices seem to have decreased risk of Alzheimer's, it isn't clear whether they actually delay the onset of disease, say experts.

In addition, researchers want to understand specifics: how much of these activities are needed, for how long and when intervention should begin to make an impact on brain health, says Bruno Vellas, a professor at the University of Toulouse Hospital.

The goal of these types of studies is to be able to offer much more specific guidance about lifestyle activities to stave off dementia, says Dr. Vellas. "With people with cognitive decline, we must be more directive."

Corrections & Amplifications

The Tommorrow study is the name of the trial funded by Takeda Pharmaceutical and Zinfandel Pharmaceuticals. An earlier version of this article called it the Tomorrow study.